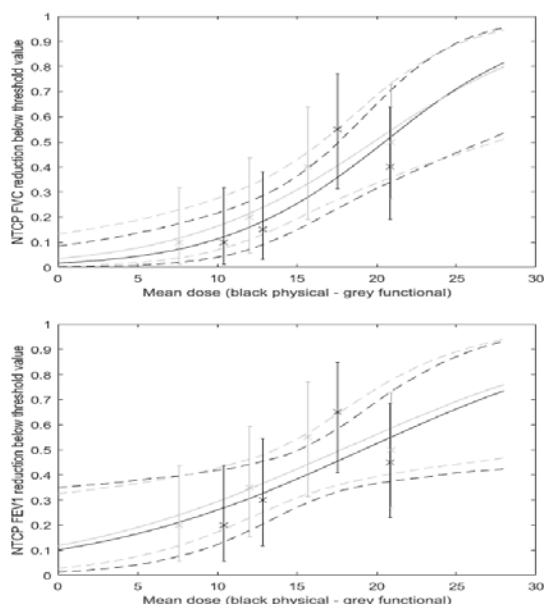


improvement in the prediction of pulmonary function loss using fMLD as opposed to MLD.

| Lung function | Physical dose | | Functional Dose | |
|---------------|---|------------------|----------------------|------------------|
| | (95% conf. interval) D ₅₀ (Gy) | V ₅₀ | D ₅₀ (Gy) | V ₅₀ |
| FVC | 20.5 (17.7-26.6) | 1.01 (0.59-1.60) | 19.8 (16.5-27.2) | 0.83 (0.46-1.32) |
| FEV1 | 19.1 (14.5-35.3) | 0.55 (0.14-1.06) | 17.8 (13.5-30.7) | 0.51 (0.18-0.89) |



Conclusion: Reduction in lung function, measured by spirometry, can be predicted by functional as well as physical lung dose, but no statistically significant difference in their predictive ability was observed in these patients. The actual biological impact of radiation on normal lung tissue might be underestimated in spirometry data (as well in patient/oncologist reported outcomes) since a significant fraction of the patients actually observe an improved lung function during treatment. This improvement is likely related to re-ventilation of obstructed airways due to tumour regression, which could mask underlying radiation damage. Another possibility is that regional ventilation may vary over a course of treatment. Analysis of 4D cone beam CT scans during treatment, and of post-treatment radiographic changes in follow-up CT scans may help untangle these "competing" effects.

Proffered Papers: Selected randomised trials

OC-0479

Neoadjuvant chemoradiation for fixed cT3 or cT4 rectal cancer: results of a phase III study

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Purpose or Objective: The study tested whether preoperative 5x5 Gy and consolidation chemotherapy is more locally efficacious than standard preoperative chemoradiation in "unresectable" rectal cancer.

Material and Methods: Patients with fixed cT3 or cT4 cancer without distant metastases were randomized either to 5x5 Gy and 3 cycles of FOLFOX4 after one week rest (experimental group) or to 50.4 Gy delivered in 28 fractions given simultaneously with two 5-day cycles of 5-Fu 325 mg/m²/day and leucovorin 20 mg/m²/day in bolus during the first and fifth week of irradiation; 5 one-day infusions of oxaliplatin 50 mg/m² were given once a week at 1, 8, 15, 22, and 29 days of irradiation. 3 cycles of FOLFOX were chosen to keep overall neoadjuvant treatment time similar in the two groups. Postoperative chemotherapy in both groups was optional. For the second study part, because of the new publications, oxaliplatin was delivered to the two groups at the discretion of the participating centre. Both randomized groups underwent surgery about 12 weeks after starting irradiation and about 6-7 weeks after completing neoadjuvant treatment.

Results: 541 patients were randomised and 515 were eligible for analysis; 261 in the experimental group and 254 in the control group of whom pelvic MR at baseline was respectively performed in 66% and 65% of patients. Oxaliplatin was given preoperatively to 70% of patients in the experimental group and to 66% in the control group, p=0.40. The incidence and severity of the neoadjuvant treatment acute toxicity was lower in the experimental group than in the control group, p=0.005; the overall toxicity rate being respectively 75% vs. 83%, grade III-IV 23% vs. 21% and toxic deaths 1% vs. 3%. The postoperative complications rate was 29% of patients in the experimental group and 25% in the control group, p=0.18. R0 resection rates (primary endpoint) and pathological complete response rates were respectively in the experimental group and in the control group 77% vs. 71% (p=0.081) and 16% vs. 12% (p=0.17). Median follow-up was 35 months. At 3 years, rates of overall survival and disease-free survival were respectively in the experimental group and in the control 73% vs. 64.5% p=0.055 and 54% vs. 52%, p=0.69. At 3 years, cumulative incidence of local failure and cumulative incidence of distant metastases were respectively 22% vs. 21%, p=0.82 and 30% vs. 27%, p=0.26. The incidence and

severity of the late complications were not different between the experimental group and the control group, $p=0.54$; the overall toxicity rate being respectively 20% vs. 21% and for grade III+ complications 9% vs. 6%.

Conclusion: The trial showed no difference in local efficacy between preoperative 5x5 Gy with consolidation chemotherapy and standard preoperative chemoradiation. Lower acute toxicity, lower cost, convenience and a trend towards improved overall survival favour 5x5 Gy with consolidation chemotherapy.

OC-0480

Five-year clinical outcome of the Phase III ACCORD 12 neoadjuvant trial in rectal cancer

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Purpose or Objective: The aim of the ACCORD 12 trial was to compare two different regimens of neoadjuvant chemoradiotherapy (nCRT). No significant difference has been found in main end point (pCR rate). At 3 years there was no significant difference for local control and survival. We report the 5 years outcome.

Material and Methods: Between 11/2005- 07/2008, 598 pts randomized. Inclusion criteria: adenocarcinoma, distal-middle rectum, T3-4, anterior-distal T2 staged using MRI and/or endorectal US. Treatment: CAP 45: radiotherapy (RT) 45 Gy/25 fr/5 weeks with concurrent capecitabine (800 mg/m² BID) vs CAPOX 50: RT 50 Gy/25 fr/5 weeks with Capecitabine (same) and weekly oxaliplatin (50 mg/m²). A TME surgery was performed after 6 weeks interval. Adjuvant chemotherapy was left to each institution.

Results: Median follow-up time was 60 months with 299 pts in each group. In intent to treat analysis main results are shown in table. In 31 pts T4 confounded the local relapse rate was 11.3%[3.8-31.5]. A clinical CR in 24 pts was associated with 81% DFS ($p<0.0001$) and Sphincter saving or organ preservation in 23. Adjuvant chemotherapy given in 253 pts.

| Endpoint | CAP 45 299 pts | CAPOX 50 299 pts | p(log rank) | HR CI 95% |
|----------------------|-------------------|---------------------|-------------|---------------------|
| Loc. Rec. 5y | 8.8% | 7.8% | 0.78% | 0.92 [0.51-1.66] |
| Dist. Met. 5y | 30% | 28% | 0.48% | 0.89 [0.77-1.15] |
| DFS 5y | 60.4% | 64.7% | 0.25% | 0.86 [0.66-1.11] |
| Overall Surv. 5y | 76.4% | 81.9% | 0.06% | 0.71 [0.50-1.01] |
| Bowel function (1-7) | 5.2 | 4.9 | NS | |

Conclusion: At 5 years there was no significant difference for local recurrence, distant metastases, survival and bowel function rates. Both CAP 45 and CAP 50 regimens are feasible and provide acceptable local control rate. More prognostic factors will be available at time of meeting and may generate hypothesis to further improve local control in locally advanced T3 or T4, achieve organ preservation in some T2 or early T3 and reduce toxicity in pts > 75 y old. Gerard Jp et al. J Clin Oncol. 2012 Dec 20;30(36):4558-65

OC-0481

Late toxicity and cosmesis after APBI with brachytherapy vs WBI: 5-year results of a phase III trial

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Purpose or Objective: The 5-year local control and survival results of the GEC-ESTRO multicentric accelerated partial breast irradiation (APBI) trial have been reported recently. In this analysis we report the 5-year late toxicity and cosmetic results of patients treated with APBI using interstitial brachytherapy (iBT) compared to those who underwent standard whole breast irradiation (WBI) with a tumour bed boost.

Material and Methods: Between April 2004 and July 2009, 1184 patients aged ≥ 40 years with stage 0, I and IIA breast cancer who underwent breast conserving surgery (BCS) were randomly assigned to receive either 50 Gy WBI with tumour bed boost of 10 Gy or APBI using HDR/PDR iBT. Among these, 5-year follow-up records on late toxicities and cosmetic results were available at 969 patients (82%). Five-year prevalences of toxicities graded by the RTOG/EORTC late radiation morbidity scoring scheme were compared using the Fisher's exact test. The cosmetic results were scored by the patients and treating radiation oncologists using the four-scale (excellent-good-fair-poor) Harvard criteria. The trial is registered with ClinicalTrials.gov, NCT00402519.

Results: There were no grade 4 toxicities. The cumulative incidence of grade (G) 2-3 late skin toxicity at 5 years was 5.7% in the WBI group versus 3.2% in the APBI group ($p=0.08$), difference: -2.4% (95% CI: -5 - 0.2%). Concerning G2-3 late subcutaneous tissue side effects at 5 years the cumulative risk was 6.3% in the WBI group versus 7.6% in the APBI group ($p=0.53$), difference: 1.3% (95% CI: -1.9 - 4.5%). The cumulative incidence of severe (G3) fibrosis at 5 years was 0.2% in the WBI group and 0% in the APBI group ($p=0.46$), difference: -0.2% (95% CI: -0.6 - 0.2%). The cumulative incidence of G2-3 breast pain was low in both arms (3.2%